DETAILED ACTION

Application Status

Claims 57, 58, 70, 71, 79, 87 and 90-93 are pending and are presented for examination on their merits.

Applicant's Arguments, filed 11/12/2009 and 03/03/2010, have been fully considered. Rejections/objections not reiterated from previous Office Actions are hereby ***withdrawn***. The following rejections/objections are either reiterated or newly applied. They constitute the complete set of rejections/objections presently being applied to the instant application.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/12/2009 has been entered.

Information Disclosure Statement

The Information Disclosure Statement filed 11/12/2009 is acknowledged and considered. The typographical errors in the aforementioned Statement have been corrected therein. The Information Disclosure Statement filed 03/03/2010 is

acknowledged and considered to the extent each reference is a proper citation on a US patent.

Applicant's Amendment

Applicant's Amendment, filed 11/12/2009, wherein claims 57, 58, 70, 71, 79 and 87 are amended, claims 1-56, 59-69, 72-78, 80-86, 88 and 89 are canceled, and claims 90-93 are added, is acknowledged.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 90-93 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of hypertriglyceridemia, does not reasonably provide enablement for other types of dyslipidemia, such as the lipid disorder hyperapolipoprotein(B). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

As stated in the MPEP § 2164.01(a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have need described. They are:

1. The nature of the invention
2. The state of the prior art
3. The predictability or lack thereof in the art
4. The amount of direction or guidance present
5. The presence or absence of working examples
6. The breadth of the claims
7. The quantity of experimentation needed, and
8. The level of skill in the art

All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

The State of the Prior Art and the Predictability or lack thereof in the art

It is noted that Applicant provides an embodiment of the treatment of dyslipidemia, in particular, hypercholesterolemia or hypertriglyceridemia, associated with low plasma level HDL, on page 8, lines 20-23, of the instant specification. With regard to treating other dyslipidemias, an undue amount of experimentation would be required to predictably practice the other treatment embodiments that are encompassed in the instant claim language. Wägner *et al.* (Diabetes Care, Vol. 22, pages 812-817; 1999) disclose on page 812, in the first paragraph of the second column, that type 2 diabetes is associated with cardiovascular disease, which might be due, at least in part, to abnormalities in lipid and lipoprotein metabolism. In the instant excerpt, Wägner *et al.* further disclose wherein diabetic dyslipidemia comprises multiple lipoprotein disorders, wherein the most typical findings are high triglyceride concentrations, low

levels of HDL cholesterol and normal or slightly increased LDL cholesterol. In the *RESULTS* section on page 812, Wägner *et al.* disclose wherein hyperapolipoprotein(B) was the most frequent lipid disorder of the study. Thus, because the instant specification does not provide enablement for hyperapolipoprotein(B), for example, it would require undue experimentation to practice the invention as broadly claimed.

The Amount of Direction or Guidance Present and Presence or Absence of Working Examples

The specification only discloses on page 14, Example 2, a study wherein anti-anthrogenic effects in patients were observed, wherein, after two weeks of therapy, the plasma levels of TC (total cholesterol) and TG (triglycerides) were reduced, and the plasma levels of HDL (high-density lipoprotein) were increased. Applicant fails to provide support for the method for the treatment of other lipoprotein disorders, e.g., hyperapolipoprotein(B), which is encompassed by the term "dyslipidemia," as set forth *supra*.

The Breadth of the Claims

The instant breadth of the rejected claims is broader than the disclosure. Specifically, the instant claims include other lipoprotein disorders of dyslipidemia, such as hyperapolipoprotein(B).

The Quantity of Experimentation Needed and the Level of Skill in the Art

While the level of skill in the pharmaceutical arts is high, it would require undue experimentation for one of ordinary skill in the pertinent art to predictably treat dyslipidemia, as broadly claimed. The science of drug development has evolved such

that without guidance or working examples in the specification, the claims lack enablement.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 57, 58, 70, 71, 79, 87 and 90-93 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 7, 14, 15, 19, 21-23, 28, 35, 36, 40, 43, 46, 50, 54 and 56 of copending Application No. 12/685,377 (hereinafter referred as Application No. '377).

Although the conflicting claims are not identical, they are not patentably distinct from each other. Application No. '377 recites a use of quaternary pyridinium salts of the formula I, e.g., 1-methylnicotinamide, for the preparation of [a] vasoprotective agent for

the treatment or prevention of conditions or diseases associated with dysfunction of vascular endothelium, oxidative stress and/or insufficient production of endothelial prostacyclin PGI_2, e.g., dyslipidemia (in particular[ly] hypertriglyceridemia in particular[ly] associated with low plasma level of HDL). Additionally, Application No. '377 recites wherein said agent is in a form for oral and parenteral administration. See reference claims 1, 2, 7, 14, 15, 19, 21, 46, 47, 50, 54 and 56. Further, Application No. '377 recites a method for treatment or prevention of the aforementioned conditions or diseases, e.g., dyslipidemia (in particular[ly] hypertriglyceridemia, in particular[ly] associated with low plasma level HDL), with 1-methylnicotinamide salt. See reference claims 22, 23, 28, 35, 36, 40 and 43.

Application No. '377 fails to recite specifically wherein the 1-methylnicotinamide salt is in the form of a composition with a pharmaceutically acceptable carrier (instant claims 79 and 93). However, in light of the specification of Application No. '377, pyridinium salts of formula I may be administered in the form of conventional oral preparations, wherein the preparations may include conventional pharmaceutical excipients and carriers. Accordingly, an artisan would have envisaged an embodiment of the instantly claimed methods wherein the 1-methylnicotinamide salt was formulated into conventional forms for oral administration, for example. See page 9, lines 17-22 of the reference specification.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NELSON C. BLAKELY III whose telephone number is (571) 270-3290. The Examiner can normally be reached on Mon - Thurs, 7:00 am - 5:30 pm (EST).

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ardin H. Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Phyllis G. Spivack/
Primary Examiner, Art Unit 1614
August 29, 2010

/N. C. B. III/
Examiner, Art Unit 1614